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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/470,944	12/22/1999	Gerard Gundling	6653.US.01	6792

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EXAMINER
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SPIEGLER, ALEXANDER H

ART UNIT	PAPER NUMBER
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1637

DATE MAILED: 01/30/2003

21

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

09/470,944

Applicant(s)

GUNDLING, GERARD

Examiner

Alexander H. Spiegler

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 26 November 2002.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1,2,4-10 and 12-16 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-2, 4-10 and 12-16 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

- 1) ☐ Notice of References Cited (PTO-892)                      4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)                      5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) \_\_\_\_\_                      6) ☐ Other:

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## DETAILED ACTION

### *Continued Examination Under 37 CFR 1.114*

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 11/26/02 has been entered. Currently, claims 1-2 and 4-10 and 12-16 are pending; claim 11 has been canceled. All arguments have been fully considered and thoroughly reviewed, but are deemed not persuasive for the reasons that follow. This action is made NON-FINAL.

### *Claim Rejections - 35 USC § 103*

2. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

3. Claims 1-2 and 4-10 and 12-16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Uematsu et al. (EP 0757106 A2, 1997), in view of Kim et al. (WO 92/18514), and further in view of Chomczynski (USPN 5,945,515).

**Uematsu et al.**

Uematsu et al. disclose a method for isolating a nucleic acid by mixing a metal oxide support, a material containing a nucleic acid, and a solution for extracting the nucleic acid forming a sample solution, separating the metal oxide support to which the nucleic acid has been bonded from the sample solution, and eluting the nucleic acid from the magnetic carrier to which the nucleic acid has been bonded (pg. 3, ln. 42-45). Uematsu et al. further teach that the solution used in the extraction of the nucleic acid contains a buffer containing a chaotropic material, such as guanidine salts, potassium iodide, sodium thiocyanate, sodium isothiocyanate, and urea (pg. 5, ln. 54-56). Furthermore, the reference teaches that the buffer can be used in combination with Triton X-100, a known detergent, and Tris HCl buffer (pg. 5, ln.56 - pg.6 ln. 1). With respect to claim 5, the reference further teaches a wash step of an aqueous solution of about 70% ethanol, following the separation of the metal oxide support/nucleic acid complex from the sample solution (pg.5, 43-44). With respect to claim 6, Uematsu et al. teach that following the wash step the nucleic acid is then eluted from the metal oxide support, with a Tris-EDTA buffer (TE buffer), or sterilized water (pg. 5, ln. 45). With respect to claim 7, the reference further teaches the detection of the nucleic acid after eluting the nucleic acid from the metal oxide support (pg. 3, ln. 57 - pg. 4, ln. 6). With respect to claim 8, the reference further teaches the step of amplifying the eluted nucleic acid (pg. 4, ln. 8-9). With respect to claim 9 and 10, the reference teaches that the nucleic acid used is RNA or DNA, and is taken from a biological source (i.e. whole blood, urine) (pg. 2-3).

Uematsu et al. teach a kit for isolating nucleic acid comprising a metal oxide support and a solution for extracting the nucleic acid, which is composed of a chaotropic agent, a detergent, and an elution buffer comprising water (pg. 4, ln. 10-12).

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With respect to claim 12, the reference teaches (pg. 14, ln. 34-35) the amplification of the nucleic acid without the removal of the elution buffer.

With respect to claims 13-14, Uematsu teaches the elution of the nucleic acid can be conducted in a solution having a low ionic strength (for example, sterilized water, which has a pH of 7.0) (pg. 6, ln. 8-9).

Uematsu fails to teach:

- 1) Immobilizing the nucleic acid by forming a bond between the nucleic acid and the metal oxide support.
- 2) A binding buffer further comprising an organic solvent, wherein the flashpoint of the binding buffer is greater than 130 degrees Fahrenheit or the use of a reducing agent.

**Kim et al.**

Kim teaches the purification of nucleic acids using metal oxide supports. Specifically, the reference teaches the bonding of nucleic acid directly to a metal oxide support material (pg. 7, ln. 11-25), which provides the advantage in that the bonded nucleic acids can be readily isolated (pg. 3, ln. 14-21), and provides the benefits of an optimal combination of such properties as recovery, relative purity, and biological activity of the recovered nucleic acid, as well as, versatility, cost, speed, simplicity, and ease of use (pg. 3, ln. 31-35).

The reference also teaches that any biological sample containing the desired nucleic acids (pg. 3, ln. 22-30). With respect to claims 15-16, Kim teaches the elution of a bound nucleic acid from a metal oxide support material using potassium phosphate (Example 5, pgs. 17-18). In

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particular, Kim teaches that 30mM potassium phosphate is effective to recover 86% of bound DNA (pg. 17).

### **Chomczynski**

Chomczynski teaches a solution for isolation of RNA, DNA, and proteins from biological material, where the solution comprises a chaotropic agent, detergent, and organic solvent (col. 10, ln. 22-34). With respect to claim 3, Chomczynski teaches that the addition of substantially lower amounts of organic solvents are required to effect the precipitation of cellular components (col. 3, ln.65-68). With respect to claims 2 and 4, Chomczynski further teaches that the solution for the isolation of RNA, DNA, and proteins, also comprises a reducing agent (see abstract, and col. 4 ln. 4). Chomczynski teaches that the reducing agent facilitates denaturation of RNase by the chaotropes and aids in the isolation of undegraded RNA.

With respect to claims 1-2 and 4-10, 12-14:

In view of the teachings of Kim, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Uematsu so as to have performed the method of separating nucleic acids from a test sample through the bonding of the nucleic acid to a metal oxide support material, in order to have achieved the benefits stated by Kim of providing a more versatile, cost-effective, and more efficient means of separation.

In view of the teachings of Chomczynski, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Uematsu and Kim so as to have added an organic solvent to the binding buffer, in order to have achieved the

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benefit of effecting the precipitation of cellular components (which would be expected to have a flashpoint of greater than 130<sup>0</sup> F); and a reducing agent to the binding buffer in order to have achieved the advantages stated by Chomczynski of enhancing the denaturation of RNase present in the sample, thereby improving the isolation of RNA from the sample.

With respect to claims 15-16, in view of the teachings of Kim, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the methods of Uematsu et al. so as to have used an elution buffer which comprises potassium phosphate in place of TE buffer in order to have provided an equally effective means for eluting the nucleic acids and providing a suitable medium for storing the eluted nucleic acid.

#### *Applicants Arguments*

4. Applicants argue:

1) There is no motivation to combine:

a) "Applicants have examined Kim...and respectfully submit that the cited paragraph of Kim is no more than unsupported "puffery." That is, Kim baldly states that the disclosed method is the best (i.e., optimal but provides no comparisons or supporting data). Even the least discriminating artisan, let alone the hypothetical "ordinary skilled artisan" would view the cited passage in Kim as an unpersuasive and unsupported self-laudatory evaluation."

b) Kim was published before Uematsu, and there is "no reasonable basis to conclude either i) that Umatsu's methods were not improved over Kim's, and ii) that Umatsu

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been unaware of Kim...and choose the methods disclosed in Uematsu in preference to those disclosed in Kim.”

2) Kim teaches the skilled artisan to precipitate or purify the nucleic acid prior to binding to the metal oxide support, which is contrary to the amended claims.

3) The rejection is based on hindsight, and that since Kim teaches that precipitation and purification must occur before binding, that the combination of Uematsu and Kim would not arrive at the claimed invention.

### *Response to Applicants Arguments*

5. Applicant's arguments have been fully considered but they are not persuasive for the following reasons:

1a) Applicants argument that Kim's teachings are “puffery” and is an “unpersuasive and unsupported self-laudatory evaluation” is clearly based on Applicants' opinion, not fact or statutory basis. The Examiner is unaware of any restriction on patent applicants, such as Kim, to avoid statements that favorably characterized their hard work. Accordingly, Applicants allegations are without foundation, and are not supported by the record.

b) First, it is noted that the obviousness rejection is based on what one of ordinary skill in the art would have been motivated to do **at the time the invention was made (i.e., at the time of filing the instant application), not at the time of Uematsu's filing.** The fact that Uematsu does not teach all of the limitations of the claim only mitigates against using this reference as an anticipatory reference. Applicants arguments are speculative as to why Uematsu did not include the teachings of Kim; this speculation is not relevant to the patentability of the instant claims.



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2) While Kim teaches examples of precipitation and purification of nucleic acids prior to binding to the metal oxide support, Kim does not teach that this is an absolute requirement of his invention. Specifically, on the bottom of page 2 and on page 26, Kim clearly teaches that the binding of nucleic acids **that have not been purified or precipitated** are encompassed in his invention. Additionally, on page 3, lines 22-26, Kim teaches that “the method is useful for any biological sample containing the desired nucleic acid, e.g., where the desired nucleic acid is present in combination with unwanted biomolecules such as other cellular components.” Applicants are interpreting the teachings of Kim too narrowly, and focusing only on a single embodiment of Kim, not on the totality of Kim’s teachings.

3) Applicants arguments are based on the allegation that Kim only teaches that precipitation or purification of a nucleic acid must occur prior to binding to the metal oxide support. However, Kim teaches that while precipitation or purification of a nucleic acid **may** occur prior to binding to the metal oxide support, it is not an absolute requirement of his method (see above).

### ***Conclusion***

6. No claims are allowable.

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*Correspondence*

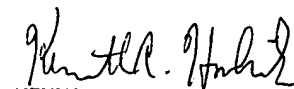
Any inquiry concerning this communication or earlier communications from the examiner should be directed to Alexander H. Spiegler whose telephone number is (703) 305-0806. The examiner can normally be reached on Monday through Friday, 7:00 AM to 3:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (703) 308-1119. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 and (703) 305-3014. Applicant is also invited to contact the TC 1600 Customer Service Hotline at (703) 308-0198.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.



Alexander H. Spiegler  
January 28, 2003



KENNETH R. HORLICK, PH.D  
PRIMARY EXAMINER

1/28/03